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The Role of Epidemiology in Informing United States Childhood Immunization Policy and Practice

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ABSTRACT

One of the ten greatest public health achievements is childhood vaccination because of its impact controlling and eliminating vaccine-preventable diseases (VPDs). Evidence-based immunization policies and practices are responsible for this success and are supported by epidemiology that has generated scientific evidence for informing policy and practice. The purpose of this report is to highlight the role of epidemiology in the development of immunization policy and successful intervention in public health practice that has resulted in a measurable public health impact: the control and elimination of VPDs in the United States. Examples in which epidemiology informed immunization policy were collected from a literature review and consultation with experts who have been working in this field for the past 30 years. Epidemiologic examples (e.g., thimerosal-containing vaccines and the alleged association between the measles, mumps, and rubella (MMR) vaccine and autism) are presented to describe challenges that epidemiologists have addressed.

Finally, we describe ongoing challenges to the nation's ability to sustain high vaccination coverage, particularly with concerns about vaccine safety and effectiveness, increasing use of religious and philosophical belief exemptions to vaccination, and vaccine hesitancy. Learning from past and current experiences may help epidemiologists anticipate and address current and future challenges to respond to emerging infectious diseases, such as COVID-19, with new vaccines and enhance public health impact of immunization programs for years to come.

Keywords: Immunization, Children, Vaccination, Health policy, Epidemiology, Health Disparities, Health Equity

List of Abbreviations and Acronyms

AAP – American Academy of Pediatrics
ACIP – Advisory Committee on Immunization Practices
AI/AN – American Indian/Alaska Native
CDC – Centers for Disease Control and Prevention
CII – Childhood Immunization Initiative
DTaP – Diphtheria and tetanus toxoids, and acellular pertussis vaccine
DTP - Diphtheria, pertussis and tetanus vaccine
FDA – Food and Drug Administration
HepA – Hepatitis A
Hib - Haemophilus influenzae type b
HHS – Department of Health and Human Services
HPV – Human papilloma virus
IIS – Immunization Information Systems
MenACWY – Meningococcal conjugate vaccine
MMR – Measles, mumps, and rubella vaccine
MMWR – Morbidity and Mortality Weekly Report
NIS – National Immunization Survey
NVAC – National Vaccine Advisory Committee
PRP-OMP – Polyribosylribitol Phosphate-Outer Membrane Protein Conjugate
Tdap – Tetanus, diphtheria and acellular pertussis vaccine
VFC – Vaccines for Children program
VPDs – Vaccine Preventable Diseases
WIC – The Special Supplemental Nutrition Program for Women, Infants, and Children

INTRODUCTION

Epidemiology is the foundation of effective immunization policy and practice in the United States . Epidemiologic methods, such as surveillance of vaccine-preventable diseases (VPDs) and vaccination coverage, risk factor identification for both disease and lack of vaccination, community intervention and effectiveness studies, and assessment of access to and quality of vaccination services have contributed to the historic reduction or elimination of many VPDs in the United States and the Americas.¹ Epidemiology has contributed to immunization policy and practice at most levels of the immunization field--from vaccine development to ensuring that vaccines reach those who need them and result in the desired public health impact, disease control, and when feasible, disease elimination. For example, surveillance and studies of childhood infectious diseases provide the basis of morbidity and mortality data used to make decisions to develop new vaccines (Figure 1). Following development of vaccines, surveillance systems have tracked vaccine effectiveness at population-level by measuring impact of vaccination in reducing disease morbidity and mortality. Similarly, surveys of vaccine coverage have been essential to monitor progress of immunization coverage levels for recommended vaccines and uptake of newly recommended vaccines, as was the case during the last decades of the 20th and the beginning of this century. Childhood vaccination science, policies and practices have contributed to reductions in disparities in VPDs through increases in vaccination coverage, particularly among low-income and racial/ethnic minority children, contributing to health equity.^{1,2} Monitoring vaccine safety through surveillance systems also has been a critical component of the immunization system in the face of vaccine hesitancy, a growing issue in the 21st century.

Immunization was selected as an example for examination of epidemiology in informing public health policy and practice because childhood immunization is one of the ten greatest public health achievements in the United States--it saves lives and is cost-effective.^{1,3-6} A study of 78.6 million children 6 years of age or younger born during 1994–2013 found that routine childhood vaccination prevented 322 million cases of illnesses and 732,000 premature deaths from VPDs, resulting in a net savings of an estimated \$295 billion in direct medical costs and \$1.38 trillion in societal costs to the United States.^{3,6}

This paper highlights the role of epidemiology in immunization policy development and public health practice that have led to major reductions in VPDs. The success of childhood immunization programs has resulted from coordinated efforts that began with a rigorous science base--including epidemiologic methods and studies--that informed decision-making, led to public health policy, and continues to guide immunization services delivery.

The working definition for policy in this paper is one generally used in public health: “a law, regulation, procedure, administrative action, incentive, or voluntary practice of governments and other institutions.”⁷ This definition can be further summarized as described by Torjman: “those decisions that seek to achieve a desired goal that is considered to be in the best interest of all members of society.”⁸

Through this examination of how epidemiology contributed to the successes, we also highlight lessons learned from immunization policy and practice that may be applicable to other public health programs, particularly those priorities delineated in Healthy People 2020.⁹

PART 1 – BACKGROUND ON VACCINE POLICY IN THE UNITED STATES

The United States has a robust policy-making apparatus for immunization policy development that supports all stages, from vaccine development to immunization practice. Many stakeholders in the public and private sector are engaged at each step--from the consideration of candidate vaccines to vaccination of children once the Food and Drug Administration (FDA) (Figure 2) license new vaccines. Many groups share responsibility in program implementation at the state, local, and even the health care office level in order to ensure high vaccination coverage, and reduction and control of VPDs.

Vaccine development requires a large and diverse research infrastructure with funding from public and private sectors that begins by identifying diseases suitable for vaccine development (Figures 1 and 2). Once a candidate vaccine is developed, rigorous testing for safety, tolerability, immunogenicity, and efficacy follows with Phase I, II and III clinical vaccine trials (Figure 1).

The private sector funds most clinical trials to demonstrate the safety, tolerability, immunogenicity, and efficacy of a candidate vaccine while the public sector funds vaccine development for selected vaccines and establishes priorities for vaccine development.

Developing new vaccines is an expensive and high-risk proposition, estimated to cost up to \$500 million dollars per vaccine and is a lengthy process, often taking more than a decade to bring a vaccine from development to market.¹⁰ The FDA in the United States plays a key role in

examining a candidate vaccine for its composition and source and the methods used for, and findings from, testing the vaccine's safety, purity and potency. Only after the FDA reviews and accepts the evidence from these initial steps, will it further examine evidence from human clinical trials about safety, tolerability, immunogenicity, and efficacy for the candidate vaccine in humans. After finding a candidate vaccine to be safe and efficacious in humans, FDA can then proceed to issue a license for the manufacture and commercial distribution for the vaccine (Figure 1).^{11,12} Once the FDA approves a vaccine, advisory committees such as the Advisory Committee on Immunization Practices (ACIP) recommend whether a new vaccine targeted for children and adults should be included in its recommended schedules for routine immunization (Figure 2).^{12,13} State and local immunization programs and health care providers play major roles in ensuring that vaccine coverage of a new vaccine quickly reaches high levels, and that established vaccines maintain a high coverage level needed to reduce or control VPDs. Professional organizations, such as the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), and the American College of Physicians (ACP), make recommendations to their members on best practices to ensure high vaccination coverage and, in collaboration with the ACIP, recommend a schedule of routine immunization. Government programs and insurance companies have a major role in the financing of vaccine purchase, and access to those vaccines. Insurance companies cover many immunizations through their health care coverage plans. Government programs, such as the Vaccines for Children Program (VFC), provide targeted funding to cover costs for all ACIP-recommended vaccines for uninsured and underinsured children ages 18 years and younger. Many stakeholders from federal, state and local agencies, health plans, hospitals, clinics, employers, health care providers and philanthropic organizations play key roles in the implementation and day-to-day operation of the United States

immunization system. The complex infrastructure of laws, regulations, funding streams, and programs continues to be informed by a spectrum of diverse epidemiologic surveillance and studies.

We now describe some key elements of the federal agencies and respective advisory committees that inform immunization policy development.

National Vaccination Policy and Federal Coordination

The National Vaccine Program Office (NVPO), provides strategic leadership and coordination among Federal agencies and other stakeholders to help reduce the burden of preventable infectious diseases.¹⁴ NVPO and National Vaccine Advisory Committee (NVAC) were established to comply with Section 2105 of the Public Health Service Act.^{14,15} NVPO obtains advice from the National Vaccine Advisory Committee (NVAC), which recommends approaches to control and prevent human infectious diseases through vaccine development, and provides advice on prevention of adverse reactions to vaccines (Figure 2).^{14,15} One example of NVAC's key role was during and after the time of the major measles resurgence of the 1990s was when it issued a call for action to eliminate endemic measles in the United States by using epidemiological evidence to improve childhood vaccination along with simultaneous monitoring of burden of measles. Use of scientific evidence by NVAC and the Advisory Committee for Immunization Practices' (ACIPs') is a strong example of how epidemiology has contributed to the development of evidence-based national policy and has strengthened the immunization system in the United States.^{13,16,17} This example is discussed later in the article.

Vaccine Development and Approval

As mentioned earlier, in the United States, vaccine development is supported by a combination of public and private sector research. In the public sector, the Federal government through the United States Department of Defense, the National Institutes of Health, and other agencies within the Department of Health and Human Services (HHS) funds vaccine development. Vaccine manufacturers invest significantly in all phases of vaccine development. The FDA is the government regulatory agency that approves vaccines for commercial use. The sponsor of a vaccine submits the required documentation on safety, efficacy, and other aspects of the candidate vaccine to the FDA. Following internal reviews, the proposal is presented to the Vaccines and Related Biological Products Advisory Committee (VRBPAC) (Figure 2), which then makes recommendations for licensing and additional data requests based on this evidence. The FDA Administrator makes the decision to approve the candidate vaccine based on the recommendation of the advisory committee. If approved, a vaccine license is issued with specific indications, precautions and contraindications.¹¹

Post-Licensure Recommendations

The Advisory Committee on Immunization Practices (ACIP), provides advice and guidance to the Director of the Centers for Disease Control and Prevention (CDC) regarding use of vaccines and related agents for control of vaccine-preventable diseases in the civilian population of the United States (Figure 2).^{12,13} Once a vaccine is licensed, and following a comprehensive review of the scientific evidence, the ACIP recommends vaccines for routine use and provides guidance on vaccine administration schedules likely to achieve the best levels of disease protection. Recommendations made by ACIP are reviewed by the CDC Director and, if adopted, are

published as official recommendations in the Morbidity and Mortality Weekly Report (MMWR).^{12,13,18} ACIP's recommended immunization schedules for children have become increasingly complex as new vaccines have been licensed as safe and effective in protecting against infectious diseases. The number of vaccines and doses have increased from 5 vaccines and 11 doses in 1989 to the current 16 vaccines and 34 doses recommended from birth to 18 years.^{13,18-20} The increased availability and recommendations for more childhood vaccines represent remarkable achievements of the maturing immunization system of the United States to prevent vaccine preventable diseases, but have contributed to growing concerns about vaccine safety acceptability.¹⁹⁻²³

The Community Preventive Services Task Force and the Community Guide

The Community Preventive Services Task Force, established by HHS in 1996, develops guidance on community-based approaches to increase vaccination coverage based on available scientific evidence.^{21,24,25} This taskforce has provided evidence-based guidance for effective community-based approaches to reach and sustain high vaccination coverage (Figure 2). Effective strategies recommended include “multi-component” efforts such as combining health care system and community interventions together, use of client reminder/recall and provider reminder systems, use of client incentives, use home visits, and implementing state or local school immunization requirements for attendance.

PART 2 - IMMUNIZATION PRACTICE AND CONTROL OF VPDs

The Role of State and Local Immunization Programs

State and local health departments, as well as tribal public health programs, provide the infrastructure for immunization services in their jurisdiction (Figure 2). Federal funding and technical assistance are provided under Section 317 of the Public Health Service Act [42 USC 243 and 42 US 247].²⁶ This law authorizes HHS to assist and advise states and their political subdivisions with matters relating to the preservation and improvement of the public's health, provide grants to states, ensure adequate supplies of vaccines, stabilize vaccine costs, and establish and maintain an accessible and efficient process for individuals found to be injured by certain vaccines.

States and local jurisdictions enact laws and regulations through their public health legal authority to require vaccinations for children enrolling in schools and childcare, that may include provisions for exemptions based on medical contraindications or philosophical or religious beliefs.²⁷⁻²⁹ School laws and regulations have been enacted in part because studies have demonstrated that they are effective community-based strategies to increase and sustain high vaccination coverage and reduce VPDs especially during outbreaks.^{28,29}

From this point on, we use the terms, “*surveillance*” and “*monitoring*” interchangeably to refer to the ongoing, systematic collection, analysis, interpretation, and dissemination of data regarding a health-related event for use in public health action to reduce morbidity and mortality and to improve health in contrast to “point in time” epidemiologic studies and outbreak investigation data use.³⁰

Surveillance of VPDs

Disease surveillance for VPDs at the state and local level is conducted under state laws and rulemaking authority using standardized case definitions developed by the Council of State and Territorial Epidemiologists in collaboration with CDC and other stakeholders. States have the legal authority to determine what diseases are considered reportable in their jurisdictions. The National Notifiable Diseases Surveillance System (NNDSS) compiles state and local data on VPDs and reports national summaries of notifiable diseases, a regular feature in the MMWR.^{31,32} CDC also monitors sporadic, endemic, epidemic and pandemic disease incidence overall and among population sub-groups to target and improve disease prevention and control efforts, including national elimination and global eradication initiatives. The recognition that HPV and hepatitis B vaccines can prevent cancer, has led to the inclusion of cancer and more recently pre-cancerous disease surveillance and registries as data sources for monitoring the impact of vaccines in reducing cervical and liver cancer, respectively.³³⁻³⁶

Monitoring Vaccination Coverage

Since the 1990s, after the resurgence of measles, the National Immunization Survey (NIS) has been measuring immunization coverage at national and state levels using standardized methods. The NIS originally targeted children 19-35 months of age, but now includes adolescents in a module designated as NIS-teen.^{37,38} The NIS (preschool child) and NIS-teen are multi-modal telephone-based surveys of parents with provider verification of immunization records. The NIS has been essential in monitoring coverage for new vaccines as they are incorporated into the recommended immunization schedule.

Monitoring Vaccine Adverse Events and the National Vaccine Injury Compensation Program

Ensuring the safety of vaccines is a key component of the immunization system. Vaccine safety and adverse event surveillance are monitored by the Vaccine Adverse Event Reporting System (VAERS), the Vaccine Safety Datalink Project, and the Post-Licensure Rapid Immunization Safety Monitoring program (PRISM).³⁹⁻⁴¹ Vaccine manufacturers also operate post-marketing surveillance systems to monitor vaccine safety based on direct reports to them (Figure 2).

During the 1980s, lawsuits related to adverse events from certain vaccines led to the withdrawal of several vaccine manufacturers from the United States market, which limited production and access to childhood vaccines. To address that challenge, the National Childhood Vaccine Injury Act [PL 99-660, 42 USC 300aa-10] was enacted. It created the National Vaccine Injury Compensation Program, a program that provides financial compensation to individuals who have been injured by a covered vaccine. Epidemiologic evidence, derived from vaccine safety surveillance and special studies, provides the scientific evidence of adverse events associated with a vaccine. Following scientific review of an event that is not already included in the Vaccine Injury Table, the National Commission on Childhood Vaccines (NCCV) advises the Secretary of HHS about the event and the HHS then publishes the rulemaking. Once an adverse event is already included in the Vaccine Injury Table, those affected can apply for compensation through a streamlined process that avoids lengthy litigation.^{42,43}

PART 3 - THE INTERFACE OF IMMUNIZATION POLICY AND PRACTICE AND EPIDEMIOLOGY

Immunization policy, practice, and epidemiology are necessarily intertwined. Epidemiology informs policy and strategies to be incorporated into immunization practice through a process

that begins with the consideration of what diseases may be preventable by a vaccine and continues with the identification of evidence-based strategies to effectively ensure high immunization coverage and optimally control or eliminate VPDs.

Epidemiology of VPDs and Vaccine Development

The development of childhood vaccines is preceded by collection and analysis of epidemiological data on the incidence of VPD-related conditions, disease morbidity and mortality, and evidence that infection confers protection against recurrence of the disease (Figure 1).⁴⁴ A recent example of this process related to the severity of varicella disease including mortality among adults in the United States prior to development of the varicella vaccine.⁴⁵

Also, as we write during the current pandemic, we are seeing unprecedented international scientific efforts to respond to the widespread community transmission of the novel Coronavirus, SARS-CoV-2, and the resulting waves of suffering and death related to COVID-19. These efforts involve the need to understand and translate knowledge about the virus and human body's immune response from transmission of COVID-19 illnesses and recovery, and to rapidly engineer, test the safety, efficacy and effectiveness, and to scale up production of new vaccines to prevent and mitigate the severity of COVID-19. Efforts in the United States include NIH's Public-Private Partnership called "Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)" and the United States Health and Human Services' "Operation Warp Speed."⁴⁶⁻⁴⁹

During vaccine development, disease surveillance and adverse event monitoring are essential epidemiological methods carried out during the conduct of clinical trials for examining the safety and efficacy of new vaccines. Data derived from clinical trials are required in the regulatory approval process leading to new vaccine availability in the marketplace. For example, Phase III field clinical trials provide efficacy data and additional safety data about candidate vaccines.^{50,51} These clinical trials are developed using rigorous epidemiologic methods, which include identifying the targeted trial population, randomization of participants to vaccination or placebo/alternative comparator groups, surveillance of the disease targeted by the vaccine, and monitoring of adverse events following vaccine administration.

Surveillance and Epidemiologic Studies of VPDs and Impact of New Vaccines

There are many examples of how epidemiologic evidence from VPD surveillance systems and outbreak investigation have contributed to better understanding of vaccine effectiveness and have led to changes in recommendations of vaccine administration. Following introduction of a new vaccine, it is necessary to measure its population effectiveness in reducing the incidence of the targeted condition. Results from ongoing surveillance of VPDs and studies of reported outbreaks also provide opportunities to investigate waning vaccine immunity, reduced vaccine effectiveness, and gaps in vaccination due to missed opportunities to vaccinate during clinical encounters and/or vaccine hesitancy. The contribution of epidemiologic studies is evident, for example, in the development of recommendations for pertussis vaccines. Studies of several pertussis outbreaks provided evidence that adults and adolescents were sources of disease transmission to young children, and that previously vaccinated adolescents were responsible for school outbreaks because of waning immunity. These findings led to additional child dose

recommendations and the development of a new acellular vaccine booster recommended for adolescents and adults.⁵²⁻⁵⁴ The evidence of both waning immunity and that vaccinated pregnant women were able to provide passive immunity to their developing fetuses, also led to recommendations for routine tetanus and influenza vaccination for pregnant women.^{53,54}

Epidemiologic studies of measles outbreaks led to the recognition that measles vaccination before 12 months of age was associated with lower vaccine effectiveness. This was the basis for the ACIP recommendation that the first measles dose be administered on or after 12 months of age.⁵⁵ Similarly, evidence from outbreaks among college students and school children showed insufficient effectiveness of a single measles dose to provide herd immunity. This led to recommendations for two doses of measles vaccines, one at 12-15 months and a second at 4 to 6 years of age.^{56,57} Other examples include a study of pertussis risk relative to the receipt and time since vaccination of the fifth dose of diphtheria and tetanus toxoids, and acellular pertussis vaccine (DTaP) during an outbreak,⁵⁸ and the role of varicella surveillance leading to change in immunization schedule from a single varicella dose to a two-dose schedule.⁵⁹ Epidemiologic studies have been used to evaluate new, and untested outbreak control interventions, such as evaluating recommendations to health care providers to vaccinate children using CDC's minimum immunization intervals during pertussis outbreaks and to use a third vaccination, during recent upsurges in mumps outbreaks.⁶⁰⁻⁶³

PART 4 – CASE STUDIES

Case Study #1 - Measles Resurgence

From 1989 to 1990, the United States experienced a major nationwide resurgence of measles, which was detected by CDC's measles surveillance. The response to these events perhaps provides the best case-study of how epidemiologic evidence has informed, refined, and redirected United States immunization policy and practice. Examination of reasons for the resurgence identified two kinds of outbreaks: (1) large outbreaks among unvaccinated preschool-aged children, mainly in large urban centers, and (2) smaller outbreaks among vaccinated children who, we know retrospectively, needed a second dose of a measles-containing vaccine.^{64,65} Additional analyses showed that unvaccinated preschool-aged outbreaks affected mostly young minority children in urban areas, with African American, Latino, and American Indian/Alaska Native children who contracted measles at rates three to 16 times higher than white children did.² The NVAC examined evidence that pointed to challenges in the United States immunization system that likely contributed to the measles resurgence and to low immunization coverage rates that were well below Healthy People 2000 objectives for preschool children. Low vaccination coverage was primarily attributed to barriers in access to vaccination services or to missed opportunities to vaccinate by health care providers.^{65,66} Cost of vaccine was a key risk factor for uninsured or underinsured children.⁶⁷ Studies indicated that children visiting health care providers did not always receive all the recommended vaccines they were due, suggesting that missed opportunities to vaccinate were also important risk factors.^{16,17,65-67} NVAC's report concluded that immunization services needed to be enhanced and expanded. To guide efforts to increase vaccination rates, the report recommended that a national, standardized surveillance system to track age-appropriate immunization coverage across jurisdictions was necessary.⁶⁸ This led to the creation of the National Immunization Survey to track the uptake of new childhood vaccines and monitor vaccination rates among young children 19-35 months of

age to guide initiatives to more completely vaccinate these children with all recommended vaccines.^{37,69-73}

The key NVAC findings and recommendations were published in 1991, in what is now considered a report of historic significance.⁷⁴ The NVAC recommendations were embraced by policy makers and resulted in the 1992 launch of the Childhood Immunization Initiative (CII).⁷⁵ The CII, a presidential initiative, included several key elements: (1) improving access to immunization services, (2) developing immunization information systems, (3) providing free vaccines to uninsured children (the Vaccines for Children Program), and (4) creating the National Immunization Program at CDC, now within the National Center for Immunization and Respiratory Diseases.

Improved Access to Immunization Services improving access required addressing missed opportunities for immunizations. At the time, there were differences in recommendations between the ACIP, the American Academy of Pediatrics (AAP) and the American Academy of Family Practice (AAFP). A major accomplishment of the CII was harmonizing the childhood immunization schedule jointly endorsed by ACIP, AAP, and AAFP, revisions of which have become a well-established convention and practice standard since 1995.¹⁹⁻²¹

To address missed opportunities, programs targeted health care providers to remind them to make every child's medical visit, including acute and chronic care visits, a vaccination visit.⁷⁶ Tools are now available to health care providers to help them assess and improve immunization practices and identify ways to eliminate missed opportunities for vaccination at their offices.

AFIX and Quality Improvement Interventions The CDC's *Assessment, Feedback, Incentive, and Exchange* (AFIX) program, is an intervention designed to assist clinics and health care provider offices to measure their immunization coverage at the practice-level and to identify missed opportunities that could be addressed through practice quality improvements. AFIX is now widely disseminated throughout the United States in all types of health care settings. Widespread use of AFIX has improved immunization practice quality and led to reductions in missed opportunities for vaccination.^{17,76,78}

Another important quality improvement intervention has been conducted through a partnership with the Special Nutrition Program for Women, Infants, and Children (WIC), a routine point of contact to reach low income, eligible children and their families that serves children nationwide.^{16,79} State and locally administered partnerships with WIC involving the assessment and referral interventions for immunizations, (preferably in a WIC clinic co-located with an immunization clinic) have been shown to be effective in improving children's immunization status.^{16,79}

Immunization Registries or Immunization Information Systems (IIS) Before the CII, most parents did not know the immunization status of their child. Use of completed immunization cards and access to scattered immunization records among child providers were very limited and there were no electronic medical records that would allow clinicians to accurately assess immunization status at every visit (something particularly difficult at emergency room visits). Immunization registries were developed to assist in the immunization assessment at each health

care visit.⁸⁰ By the mid-1990s, provider-based and population- or community-based immunization registries, now called Immunization Information Systems (IIS), were created for use by health providers to address immunization record scatter across clinics. IIS are powerful and effective tools that provide timely access to immunization status at the point of care and have reduced missed opportunities by targeting under-vaccinated children for vaccination reminders and recalls, even before the introduction of electronic health record (EHR) systems.⁸¹⁻⁸³ A successful example of how immunization registries can assist immunization efforts across jurisdictions was their effective use in interstate data sharing of vaccine records to facilitate school enrollment of displaced school children during Hurricane Katrina recovery efforts.⁸⁴

The Challenge of Vaccine Cost The Vaccines for Children (VFC) program addresses the barrier of vaccine cost by providing all ACIP-recommended vaccines at no cost to children 18 years of age and younger if they are Medicaid eligible, uninsured, are American Indian or Alaska Native, or underinsured and receive immunizations at a Federally Qualified Health Center or Rural Health Clinic.⁸⁵ In addition to the VFC program, the limited, discretionary immunization grant program to states, known as 317, covers children, adolescents and adults not eligible for VFC.²⁶

Monitoring Vaccination Coverage for Decision Making Prior to the measles resurgence, quarterly estimates of vaccination coverage at the national level were provided by the National Health Interview Survey (NHIS), a probability sample survey of the civilian, noninstitutionalized United States population.⁸⁶ At the time, there was limited monitoring of preschool child vaccination coverage at the state level.⁸⁷ There was an ongoing effort by states to monitor vaccine coverage among school-aged children, but this surveillance approach focused on state–

required vaccination status at the time of admission to schools and day care. Preschool child vaccination monitoring was limited to either retrospective evaluations of vaccination histories reported at the time of school entry, which included vaccinations that may have been given four or more years previously only among children remaining in the area at school entry or state or local-based birth certificate follow back surveys.⁸⁸ In 1994, the telephone-based National Immunization Survey (NIS) with provider verified immunization record reports was developed to monitor immunization coverage of children less than 36 months old for states and selected large cities.^{37,87-89} In addition to measuring coverage of individual vaccines, NIS developed standardized measures of completeness of recommended single vaccinations and combined series of vaccines, such as completing four doses of DTP, three doses of polio, and one dose of measles, mumps, and rubella vaccine (MMR) (4:3:1).^{72,88-90} As new vaccines were added to the immunization schedule, the combined series have been expanded.⁷² Table 1 includes a glossary of selected measures of vaccine completeness.^{72,89}

The ACIP expansion of recommended vaccines to adolescents and adults led to upgrades of the NIS to specifically measure vaccination coverage for adolescents, including tetanus-diphtheria-acellular pertussis (Tdap) and meningococcal conjugate vaccine (MenACWY), by creating the NIS –Teen module in 2006.^{38,91,92} In 2007, monitoring for human papillomavirus (HPV) vaccination was added. Like the original preschool child NIS, this NIS adolescent module includes provider-verified receipt of vaccines rather than relying on self-reported vaccination and provides data at state and selected local levels. Vaccination coverage among young children and adolescents is found in Figure 3 and Tables 2 and 3.

Case study #2 - Vaccine Hesitancy in the Era of VPDs Control and Elimination

The end of the 20th century and the subsequent decades of the 21st century have witnessed further declines and the control of many VPDs. Polio has been eliminated from the Americas and most of the world and it is near eradication worldwide. Diseases like diphtheria, tetanus, measles, rubella, mumps, *Haemophilus influenzae* type b and others have been either eliminated or controlled as a result of effective vaccines and comprehensive strategies to promote high vaccination coverage among children, adolescents, and more recently, adults. A consequence of this success is that most people, including health care providers, have not seen or treated a case of those diseases and have not experienced their serious morbidity and mortality.⁹³ This lack of awareness of the morbidity and mortality of VPDs have contributed to parental vaccine hesitancy.^{23,94,95} In fact, in a population-representative survey, Kempe et al estimated that 1 in 15 United States parents are hesitant about routine childhood vaccines and more than 1 in 4 United States parents were hesitant about childhood influenza vaccines.⁹⁶ Issues related to thimerosal preservative in vaccines, and the publication of an article 20 years ago alleging an association between MMR and autism, later retracted, added to parental concerns about the safety of and need for child immunization and have resulted in an increase in the number of children who are not vaccinated or only partly immunized.⁹⁷⁻⁹⁹ Vaccine hesitancy has grown into a worldwide phenomenon leading the World Health Organization (WHO) in 2019 to declare vaccine hesitancy as one of the ten threats to global health.¹⁰⁰

Thimerosal and Autism Thimerosal, a preservative that contains ethyl mercury, was used in over 30 United States-licensed and marketed vaccines. This preservative was added to prevent

bacterial contamination in multi-dose vials because of the risk of bacterial contamination each time a needle is inserted in the vial.⁹⁷ The Food and Drug Administration Modernization Act of 1997 required that the agency examine adverse effects from exposure to mercury on the health of children and other sensitive populations. This led to a review of all approved vaccines and other FDA-approved products that contained organic mercury. The review found no evidence of adverse events from the doses used in approved vaccines, but did find that “use of thimerosal as a preservative in vaccines might result in intake of mercury during the first six months of life that exceeds the Environmental Protection Agency, but not the federal Agency for Toxic Substances and Disease Registry, FDA, or World Health Organization guidelines for methyl mercury intake.”¹⁰¹ This finding led the United States Public Health Service agencies and the American Academy of Pediatrics (AAP) to issue a statement to clinicians recommending that thimerosal be reduced or eliminated from vaccines *as a precaution*.¹⁰² By 2001, all recommended childhood vaccines in the United States, except for some forms of the influenza vaccine, were thimerosal free. Several studies were conducted to examine the potential risk of thimerosal exposure in early infancy and the risk of neurodevelopmental disorders. Published studies have provided strong evidence against neurodevelopmental effects resulting from thimerosal.¹⁰³ Furthermore, despite the removal of thimerosal from childhood vaccines, the estimated prevalence of autism within select communities in the United States has continued to increase, from 6.7 per 1,000 for 8 year olds in 2000 to 14.6 per 1,000 in 2012.¹⁰⁴

MMR and Autism A major source of vaccine safety concerns among some parents derived from the now discredited 1998 *Lancet* journal article by Andrew Wakefield et. al., which suggested a link between the MMR vaccine, ileal-lymphoid-nodular hyperplasia and autism

among a small group of selected case-patients with no control patients.⁹⁸ In 2004, 10 of the 13 original authors retracted their participation in the article and the *Lancet* retracted the article in 2010.⁹⁹ In spite of the retraction, this article created major concerns among parents considering vaccinating their children and continues to affect vaccination coverage of the MMR vaccine. A large epidemiologic study in Denmark provided strong evidence of a lack of association between MMR and autism.¹⁰⁵ Similarly, a study in the United Kingdom did not find any association between MMR and autism.¹⁰⁶ The Institute of Medicine in the United States examined all available evidence and concluded that there was no evidence to link MMR vaccination and autism.¹⁰⁷

The consequences of the subsequently retracted Wakefield article include dramatic initial declines in MMR vaccination coverage in some countries. There were numerous resulting outbreaks of measles and mumps in the United Kingdom, France, and elsewhere.¹⁰⁷⁻¹¹⁰ Surveillance documented that, in 2014, the United States experienced 667 cases in 27 states, the largest number of measles cases since endemic measles was eliminated in 2000.¹¹¹ Nearly all case-patients were unvaccinated. Limited local transmission in the United States occurred following the introduction (or importation) of measles from 22 different countries indicating the presence of some pockets of measles susceptibility. Communities with less than adequate vaccination rates were at particularly high risk for rapid disease spread when measles was introduced.

These recent cases and outbreaks provide new insights about the prevention and control of measles. The public's perception about vaccine risks and the lack of memory or experience with

the adverse consequences of measles and other vaccine-preventable diseases have likely contributed to vaccine hesitancy in some populations.⁹⁴⁻⁹⁶ The NIS has shown a shift of unvaccinated and under-vaccinated from uninsured and low socioeconomic status children to children who are insured and of higher education and socioeconomic status. Such changes make evident the need for greater understanding of the factors influencing parents' decision to not vaccinate their children, and its impact in measles control and elimination.¹¹² To address parental vaccine hesitancy, CDC and state and local epidemiologists have increased efforts to monitor vaccination coverage and study risk factors for parent personal-belief exemptions to school immunization requirements.⁹⁵ Studies continue to document outbreaks and increased incidence of VPDs, such as measles and pertussis, associated with vaccine hesitancy in United States communities.^{58,113-123} Wolf et al. found that, unlike during many outbreaks, vaccine uptake did not increase during Washington's statewide pertussis outbreak.¹¹⁶ Noting that vaccination promotion is an important outbreak control measure, Wolf et al. examined the literature on key potential factors related to vaccine uptake, such as the public's risk perception, trust, media coverage during epidemics and vaccine hesitancy. They proposed a conceptual model for designing interventions to increase vaccine uptake during outbreaks, including addressing vaccine hesitancy. They also strongly recommended that such measures be studied to provide needed evidence for outbreak control in the future.¹¹⁶

Religious, Philosophical and Non-Medical Exemptions In the late 1990s and early 2000s, parent claims of religious, philosophical and non-medical exemptions to school immunization requirements increased, signaling that changes in parental attitudes about vaccinations were occurring.^{95,120} In Colorado and Oregon, exemptions increased well beyond the average

percentage of less than one percent seen in previous years. Further investigations in communities such as Ashland, Oregon, where grade school exemptions were substantially high (15% by 2004 and 2005), suggested that exempting parents likely clustered together and relied on information from sources other than the traditional health care establishment.^{95,124} Follow-up studies in Oregon and other communities confirmed that multiple factors were associated with parent exemption claims and that community and individual factors were equally important.^{95,124} These and other studies suggested that health care providers needed to be more informed about vaccinations, listen to parental concerns, and discuss vaccine safety with parents. Again, this is an example of how epidemiologic data can impact immunization practice at the point of service. Studies to examine reasons for intentional delay of recommended vaccines are key to understanding current vaccine disparities and the characteristics of those who delay or refuse vaccines in order to develop effective strategies to address this major challenge to the control of VPDs.

The NIS is providing key data which can be used to monitor rates of unvaccinated two-year-old children among states and regions in the United States. For example, Oregon and Washington were among the states with the lowest vaccine coverage (combined vaccine series) for two year-old children in 2013.¹²⁵ NIS has also confirmed other study findings that suggest that those who intentionally delayed vaccination are significantly more likely to have heard or read unfavorable information about vaccines than parents who did not intentionally delay.¹²⁶ Additionally, parents who intentionally delayed due to vaccine safety or efficacy concerns were significantly more likely to seek information from the internet rather than from a health care provider compared with parents who delayed because of child illness. Differences by race have been documented in

these analyses--the percentage of parents who intentionally delayed immunizations was highest among White, Non-Hispanics (28.1%), American Indian/Alaska Natives (26.6%), followed by Asians (17.2%), Hispanics (14.5%), and Blacks (12.4%).¹²⁶ Further analyses are needed to evaluate which parental, community and other characteristics and risk factors underlie these notable differences by racial/ethnic groups in childhood vaccine delays, for example examining how differences in historical experiences with VPDs and trust may influence vaccine decision making among different groups. Findings about intentional delays in immunization among some 2-year-old children and the ability of parents to claim religious or philosophical exemptions raise questions about the influence of the ease of parent claims in some states and higher state vaccination exemption rates. One study found that states enacting stricter exemption policies tend to have lower rates of exemptions.¹²⁰ In recent years, Congress and states, such as California, Vermont, Utah, Washington and Oregon, have passed or attempted to pass laws to modify or eliminate the use of non-medical exemptions.¹²⁷⁻¹³⁵ These policy initiatives are being met with public controversy and opposition by nationally-organized and grassroots groups communicating vaccine safety, civil liberty, other concerns, and also anti-vaccine sentiments.¹²⁷⁻

¹³¹ The legal viability and public health effectiveness of these more restrictive strategies remain to be determined. Early studies of California's non-medical exemption elimination show that, while non-medical exemptions declined, geographic clustering of these exemptions remained leaving populations of students at-risk for VPDs in a number of communities.¹³²⁻¹³⁴

Epidemiological studies clearly play a key role in monitoring changing child immunization coverage, non-medical exemptions to school immunization requirements and other measures of vaccine hesitancy trends and the impact of policy changes and the interventions to address them.

Case Study #3 - Vaccines and Special Populations

Another important immunization practice issue is addressing differences in VPD morbidity and disparities in vaccination coverage among special populations. Epidemiological studies proved to be particularly relevant when examining the impact of *Haemophilus influenzae* type b (Hib) and hepatitis A (HepA) vaccines on the American Indian/Alaska Native (AI/AN) population.¹³⁵ The introduction of the Hib vaccine significantly reduced Hib incidence in AI/AN children.

Surveillance proved to be critical in demonstrating a greater response with the first dose of the polyribosylribitol phosphate conjugated to the meningococcal outer membrane protein (PRP-OMP)-containing Hib vaccines for AI/AN infants providing earlier protection. In fact, when Alaska switched from PRP-OMP to non-OMP vaccine during a vaccine shortage, AI/AN Hib incidence increased.^{136,137} Again, epidemiological evidence was important to guide immunization practice.

Besides experiencing higher Hib disease incidence, AI/AN children historically had more than a five-fold higher incidence of HepA virus infection and were experiencing frequent large-scale outbreaks every 10-15 years. With the implementation of routine HepA vaccination in 1995 among high-risk populations (e.g., AI/ANs), disease incidence and outbreak disparities were completely eliminated.¹³⁵

As another special population, the Amish were the last group to experience a polio outbreak in the United States. In 2000, Pennsylvania noted an increase in Hib disease among Amish preschool children. An epidemiologic study of Hib carriage showed high levels of Hib carriage and low vaccination coverage among Amish households. A study among Amish parents who did

not vaccinate their children found that only 25% identified personal-belief objections as a factor, 51% reported that vaccination was not a priority compared with other daily activities, and 73% would vaccinate children if offered locally.¹³⁸ These findings encouraged the state to target Hib vaccination programs to Amish communities and craft specific educational messages to Amish parents leading to a reduction in Hib disease in this special population.

These examples show how public health used epidemiologic surveillance to document increases in disease incidence and disparities in vaccination coverage in special populations in order to respond with targeted interventions to address these problems and achieve disease prevention successes.

Case Study #4 - Introducing New Vaccines: Identifying Barriers and Enhancers to Rapid Uptake

Epidemiologists are improving their methods to track new vaccine uptake, especially for newer vaccines including the multi-dose human papillomavirus (HPV) vaccine to prevent cervical cancer and the Tdap booster for adolescents and adults.

Since 2007, NIS-Teen has provided valuable information for newer vaccines such as Tdap, MenACWY, and HPV. NIS-Teen data showed for at least one dose, initial vaccine uptake rose considerably among those 13-17 years of age; for MenACWY, rates rose from 11.7% in 2006 to 86.6 % in 2018; and for Tdap rates rose from 10.8% in 2006 to 88.9% in 2018.^{91, 92} For HPV, both initiation with at least one dose and completion rates were tracked through NIS-Teen. During 2007, the first year that HPV was recommended for girls, uptake with at least one dose of HPV vaccine for 13-17-year-old girls was 25.1%.⁹¹ By 2018, HPV initiation had risen to 69.9%

for 13-17 year old girls.⁹² Rates of HPV completion for girls (receipt of at least three doses) began at 17.9% of girls in 2008.⁹¹ By 2018, the completion rate was 53.7% overall with increasing rates by age from 38.9% completion among 13-year-old girls to 66% among 17-year-old girls.⁹² Rates of HPV initiation (66.3% in 2018) and completion (48.7% in 2018) are lower for 13-17-year-old boys, partially reflecting the later release of ACIP recommendations for HPV vaccination of males (2011).^{91,92}

The HPV Vaccine Experience Epidemiologists have looked closely at the factors associated with rates of HPV vaccine initiation and completion to examine vaccine uptake and acceptance.¹³⁹ Observed differences pointed out that further research was needed to better understand population-specific barriers to completion of the HPV series.

Monitoring HPV uptake, first among adolescent girls and later among adolescent boys, epidemiologists focused on identifying risk factors associated with low HPV vaccination. A 2009 telephone survey of mothers of 11-17-year-old girls found that the predominant perception was that their daughters were at low risk for HPV infections and HPV-related diseases. Findings also showed that mothers and their health care providers lacked sufficient knowledge about HPV disease and HPV vaccines.¹³⁹ Many mothers also reported that they believed that their daughters were currently too young to receive the HPV vaccine although receipt might be more acceptable at later ages. Also, mothers reported significant concerns about the long-term safety of these vaccines. The most commonly identified reasons for mothers accepting these vaccines for their daughters included: their perceptions that their daughters were at high risk for acquiring HPV; their beliefs that the vaccine had a favorable safety profile; their intentions to prevent cervical

cancer among their daughters and protect them against cancer; their own personal experience with HPV infection or HPV-related diseases; and their recalling strong physician recommendations to vaccinate their daughters.¹⁴⁰ These findings have been shaping the messages and strategies to promote HPV vaccination with a stronger focus on the cancer prevention benefit of this vaccine.

Case Study # 5: - Impact of COVID-19 Pandemic: Immunization Coverage and COVID-19 Vaccine Acceptance

As in other countries, the impact of the COVID-19 pandemic on the United States immunization system and policies is starting to become apparent as COVID-19 continues to rapidly spread across communities. Since public health authorities across the United States have needed to urgently implement non-pharmaceutical public health disease containment measures (e.g., shelter-in-place, postponements of noncritical health care visits), early epidemiological studies are already documenting a dramatic decline in ordering and administration of childhood vaccines, VFC clinic capacity to vaccinate children, and immunization coverage rates for VPDs.¹⁴⁰⁻¹⁴⁷ Rapid development of new COVID-19 vaccines is an imperative because of the severe consequences of COVID-19 disease, which is disproportionately impacting people over 60 years of age, people with heart disease, diabetes, other chronic diseases, essential service workers and populations of color.⁴⁶⁻⁴⁹ However, as new vaccines for COVID-19 are being developed and tested, new reports also suggest the emergence of major challenges for new COVID-19 vaccination uptake.¹⁴⁸⁻¹⁵⁰ Several reports state that that up to 33% percent of polled respondents were hesitant about accepting new COVID-19 vaccines when they become available.^{149,150}

Previous epidemiological studies have shown that after vaccine supply chain disruptions and shortages have occurred, uptake of vaccine may slowly recover and could remain persistently lower than prior uptake well behind recommended target coverage rates when supplies become available. Re-engaging patients for clinical preventive services and increasing vaccination among people who have previously declined or fallen behind schedule during and after the COVID-19 crisis are critical strategies to prevent other VPD outbreaks, which could further strain our health care system, emergency response systems, and economy and, thus, slow economic and societal recovery from the pandemic.^{143-145,151}

With delays in vaccinations, vaccine hesitancy and upcoming seasonal influenza transmission, during the pandemic, we face new challenges that risk losing historical achievements in individual and community health and new unknown risks of further preventable illnesses, disabilities and death.^{116,152-155} Previous epidemiologic evidence suggests that by reducing the incidence of VPDs such as influenza and pneumococcal disease, we also would reduce burden on the health care facilities that are already under pressure in communities responding to the waves of COVID-19 outbreaks and community-wide transmission. Immunization policy makers, public health practitioners and health care providers must plan new immunization initiatives that include proactively and transparently gaining back the trust of an already skeptical public whose trust in public health and health care advice during this pandemic have been sorely tested.^{116,148-150} Epidemiologic surveillance, research and program evaluation will be essential nationally, regionally and within communities to guide needed interventions that successfully respond to these new public health challenges.

PART 5 - FUTURE DIRECTIONS

Recent challenges to the immunization system come from diverse sources, such as the need for new vaccines to prevent dengue, Zika, Ebola and, now, COVID-19 disease, and vaccine shortages.¹⁵⁶ There is also a need to better inform and convince parents, health care providers, and the general public about the safety and benefits of immunizations in this era where some VPDs have not been experienced in years and the memory of their devastating effects has been forgotten or never encountered. Many epidemiologists are working to design studies aimed at understanding how to more effectively promote behavior change and translate the results of current vaccine studies to inform wider audiences of stakeholders, including patients and health care providers. As credible scientists, epidemiologists can take leading roles in focusing on research and interventions that answer important questions, improve understanding, and address concerns regarding the safety, efficacy and effectiveness of vaccines well beyond the studies used by FDA for licensing. Focused research to better address vaccine hesitancy, and health services research including implementing operational research, program evaluation, economic analyses, health equity studies, rapid-cycle quality improvement, and research on rare events, can be helpful. These research endeavors can include studies of patient and provider knowledge, beliefs, attitudes and behaviors or practices and the effectiveness of interventions with culturally and linguistically appropriate services in health and health care.

Further enhancements to more rapid global monitoring, interventions and elimination and eradication goals and strategies are needed to prevent and mitigate importation of vaccine-preventable diseases across borders. To obtain generalizable vaccine safety evidence, even larger linked databases are needed to monitor for and study rare vaccine adverse events. Ongoing surveillance and monitoring of vaccine supplies are needed, especially in cases of outbreaks in

children (e.g., 2004 flu vaccine shortage). Ongoing monitoring is also needed to inform planning and regulate vaccination costs, to expand and target child and adult vaccinations, and for early detection of previously locally eliminated, or new variant illnesses potentially caused by unusual or rare infectious agents including those intentionally introduced as biological weapons such as smallpox or anthrax.

More challenging is the ongoing need to develop new, specific vaccines for emerging diseases with high morbidity and mortality and rapid spread as real-time countermeasures, notable at the time of this writing during the COVID-19 pandemic.^{46-49,148,155} Especially challenging is that currently governments are usually the sole funding source for vaccine development unless commercial manufacturers offer to help and see financial and other incentives including the potential for more routine population-wide use.^{46-49,155-157} To be ready to respond effectively to the eventuality of new, emergent vaccine-preventable outbreaks and community-wide biological attacks, policy makers, health officials, legislators and other stakeholders can work together to ensure that policies are in place to expedite development of new vaccines, ensure vaccine safety and efficacy, and determine appropriate resources in a timely fashion. Public/private partnerships can be developed to meet the demands for research and development of new vaccines and to establish capacity for production. Additional public health system capacity across all levels and communities could be enhanced and sustained in order to address mass vaccine distribution and administration by health care providers, vaccination monitoring, disease surveillance, and program and policy evaluations to meaningfully inform policy and program decisions in real-time.

Uniform, quick, appropriate and timely reporting of disease cases and adverse events by physician offices, hospitals, laboratories, schools or other institutions such as child-care and correctional facilities can be more firmly established. Enhanced electronic reporting from electronic laboratory and health record systems, data analyses and information dissemination can be enhanced to function more rapidly in real-time. Rapid surveillance using electronic data is needed to provide more timely and accurate situational status assessments, target services and improve response time to public health emergencies.

Epidemiologists can expand their use of methods from other public health disciplines, such as community-based participatory research, qualitative research, rapid-cycle quality improvement work and evaluation methods to better identify vaccine acceptance disparities and differences in perceptions, knowledge, attitudes, and beliefs among specific populations, including providers. Interventions that overcome the barriers and address the needs of special populations can be developed, implemented, evaluated and disseminated.

Conclusions

Epidemiology remains essential for informing policy and programmatic practice decision making to prevent and respond to VPDs. Epidemiologic studies of the large United States measles resurgence identified major factors by further identifying determinants of low vaccination coverage. These efforts were crucial for focusing policies and programmatic strategies at national, state and local levels. Surveillance and epidemiologic research have also been essential in monitoring the impact of vaccinations on infectious disease incidence and vaccine acceptance

by clinicians, parents and patients. While epidemiology has positively influenced changes in immunization policy and led to historic reductions in VPDs, the reduction of VPD incidence has created new challenges in our ability to help parents and providers understand why vaccines remain essential. Recent developments have led to public questioning of the value and risks of vaccinations while vaccine acceptance is high.^{23,94-96,116,126,149,150,158} However, the nation must be vigilant in continuously measuring vaccine use, vaccine-preventable diseases, and vaccine safety, to avoid the trap of being victims to our own success.

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Role of Epidemiology in Informing US Childhood Immunization Policy
Tables/Figures

Table 1. Definition of combined vaccine series measures and vaccination coverage estimates for children 19-35 months of age: United States, 2017

Definition of Combined Vaccine Series Measures ¹	Measure abbreviations	Vaccination Coverage (2017) ² % (95% CI)
≥4 DTP/DTaP: ≥3 Polio: ≥1 MMR	4:3:1	81.7 (80.5-82.9)
≥4 DTP/DTaP: ≥3 Polio: ≥1 MMR: ≥3 Hib	4:3:1:3	75.8 (74.4-77.1)
≥4 DTP/DTaP: ≥3 Polio: ≥1 MMR: ≥3 Hib: ≥3 HepB	4:3:1:3:3	74.2 (72.7-75.6)
≥4 DTP/DTaP: ≥3 Polio: ≥1 MMR: ≥3 Hib: ≥3 HepB: ≥1 Varicella	4:3:1:3:3:1	73.2 (71.7-74.6)
≥4 DTP/DTaP: ≥3 Polio: ≥1 MMR: ≥ Hib Full Series: ≥3 HepB: ≥1 Varicella: ≥4 PCV	4:3:1:3:3:1:4	70.4 (68.9-71.9)

Abbreviations: DTP/DTaP = diphtheria and tetanus toxoids and whole cell pertussis vaccine or diphtheria and tetanus toxoids and acellular pertussis vaccine; Polio = poliovirus vaccine; MMR = measles-mumps- rubella vaccine; Hib = *Haemophilus influenzae* type b vaccine; Hep B = hepatitis B vaccine; Varicella= varicella vaccine; and PCV = pneumococcal conjugate vaccine.

Table 2. Vaccination coverage among children ages 19-35 months, by selected vaccines and dosages* and race/ethnicity – National Immunization Survey, United States, 2017)²

Vaccine	Dosage	Race/Ethnicity						
		Non-Hispanic White	Non-Hispanic Black	Hispanic	American Indian/Alaska Native only	Asian only	Native Hawaiian/ Other Pacific Islander only	Two or More Races
		% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
DTaP	≥ 4 doses	86.1 (84.7-87.3)	78.2 (73.8-81.9)	81.7 (77.4-85.3)	79.5 (69.1-87.0)	88.1 (83.6-91.5)	87.8 (79.3-93.1)	83.1 (76.9-87.9)
Polio	≥ 3 doses	94.0 (93.0-94.9)	93.3 (89.6-95.7)	93.4 (91.9-94.6)	90.1 (81.9-94.8)	95.2 (91.9-97.2)	92.3 (84.8-96.3)	91.8 (88.4-94.3)
MMR	≥ 1 dose	91.7 (90.2-93.0)	91.4 (87.7-94.1)	92.8 (91.3-94.1)	90.2 (82.1-94.8)	94.9 (91.5-97.0)	93.1 (85.7-96.8)	91.9 (88.5-94.4)
Hib	Full series	84.5 (82.9-85.9)	77.1 (72.6-81.0)	81.0 (77.1-84.4)	83.7 (74.4-90.1)	83.6 (76.2-89.0)	85.8 (76.5-91.8)	79.8 (73.6-84.8)
HepB	≥ 3 doses	92.7 (91.6-93.7)	90.7 (86.8-93.5)	92.2 (90.1-93.9)	90.0 (81.7-94.8)	90.9 (83.0-95.4)	93.2 (85.8-96.9)	92.2 (88.9-94.6)
Varicella	≥ 1 dose	91.4 (90.2-92.5)	91.0 (87.3-93.8)	93.3 (91.8-94.5)	89.3 (80.5-94.5)	94.6 (91.4-96.7)	92.9 (85.5-96.7)	91.2 (87.8-93.7)
PCV	≥ 4 doses	85.5 (83.8-86.9)	79.0 (74.6-82.9)	81.9 (77.8-85.3)	80.1 (70.4-87.2)	81.0 (73.5-86.8)	88.1 (79.7-93.3)	82.1 (75.9-87.0)
HepA	≥ 2 doses	63.7 (61.6-65.7)	56.7 (52.0-61.3)	62.9 (58.9-66.8)	NA	62.7 (55.0-69.9)	NA	59.5 (52.6-66.0)
Rotavirus	≥ 2 or ≥ 3 doses	78.8 (77.0-80.4)	67.8 (63.2-72.1)	71.0 (66.6-75.1)	NA	75.2 (66.2-82.5)	NA	73.6 (67.3-79.0)
Combined 7-vaccine series**		75.0 (73.1-76.9)	67.9 (63.3-72.2)	70.4 (66.2-74.4)	73.0 (62.1-81.7)	73.6 (66.2-79.9)	85.2 (75.9-91.4)	74.2 (68.0-79.5)

Abbreviations: DTP/DTaP = diphtheria and tetanus toxoids and whole cell pertussis vaccine or diphtheria and tetanus toxoids and acellular pertussis vaccine; MMR = measles- mumps-rubella vaccine; Hib = *Haemophilus influenzae* type b vaccine; HepB = hepatitis B vaccine;

Varicella=varicella vaccine; PCV = pneumococcal conjugate vaccine; HepA = hepatitis A vaccine; Rotavirus = rotavirus vaccine.

*Selected vaccines and dosages are in accordance with immunization objectives from *Healthy People 2020*³ and follow the CDC's recommended immunization schedule for children and adolescents ages 18 years or younger⁴

**The combined 7-vaccine series (4:3:1:3*:3:1:4) includes ≥ 4 doses of DTaP, ≥ 3 doses of poliovirus vaccine, ≥ 1 dose of measles-containing vaccine, the full series of Hib (≥ 3 or ≥ 4 doses, depending on product type), ≥ 3 doses of HepB, ≥ 1 dose of varicella vaccine, and ≥ 4 doses of PCV.

Table 3. Vaccination coverage among adolescents ages 13-17 years, by race/ethnicity and selected vaccines and doses*⁴ – National Immunization Survey – Teen, (NIS – Teen), United States, 2018†⁵

Vaccine	Dosage	Race/Ethnicity					
		White (Non-Hispanic)	Black (Non-Hispanic)	Hispanic	American Indian/Alaska Native (Non-Hispanic)	Asian (Non-Hispanic)	Multiracial (Non-Hispanic)
		% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Tdap	≥ 1 dose	89.7 (88.7-90.6)	88.4 (85.9-90.5)	87.7 (85.4-89.7)	86.4 (78.7-91.6)	87.9 (80.9-92.6)	89.0 (85.5-91.7)
MenACWY	≥ 1 dose	86.0 (84.9-87.1)	87.1 (84.5-89.3)	87.6 (85.2-89.7)	82.6 (74.3-88.6)	85.9 (77.8-91.3)	87.1 (83.7-89.8)
HPV	≥3 doses or 2 doses**	47.8 (46.2-49.4)	53.3 (49.4-57.2)	56.6 (53.4-59.8)	57.3 (47.0-67.0)	53.1 (44.7-61.3)	51.1 (45.5-56.6)
MMR	≥2 doses	92.8 (91.9-93.5)	93.1 (91.3-94.6)	89.9 (88.0-91.5)	91.6 (84.9-95.5)	89.0 (80.0-94.2)	92.5 (89.1-94.8)
HepB	≥3 doses	93.2 (92.2-94.0)	93.1 (91.2-94.6)	89.1 (86.9-91.0)	92.9 (87.2-96.2)	93.3 (89.7-95.7)	92.1 (88.6-94.6)
Varicella***	≥ 2 doses	90.8 (89.8-91.7)	89.4 (86.0-92.0)	87.6 (85.5-89.5)	89.9 (81.7-94.7)	86.1 (76.2-92.3)	90.3 (86.7-93.1)

Abbreviations: Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; MenACWY = meningococcal conjugate vaccine; HPV = human papillomavirus vaccine; MMR = measles- mumps-rubella vaccine; and HepB = hepatitis B vaccine.

† For information by poverty level, see the original article: Walker et al, 2019⁵

*Selected vaccines and dosages are in accordance with immunization objectives from *Healthy People 2020* and follow the CDC's recommended immunization schedule for children and adolescents aged 18 years or younger.^{3,4}

**Includes those with ≥3 doses, and those with 2 doses when the first HPV vaccine was initiated prior to age 15 years and there was at least five months minus four days between the first and second dose.

***Among adolescents with no history of varicella.

Figure 1. Role of epidemiology in childhood immunization policy and practice

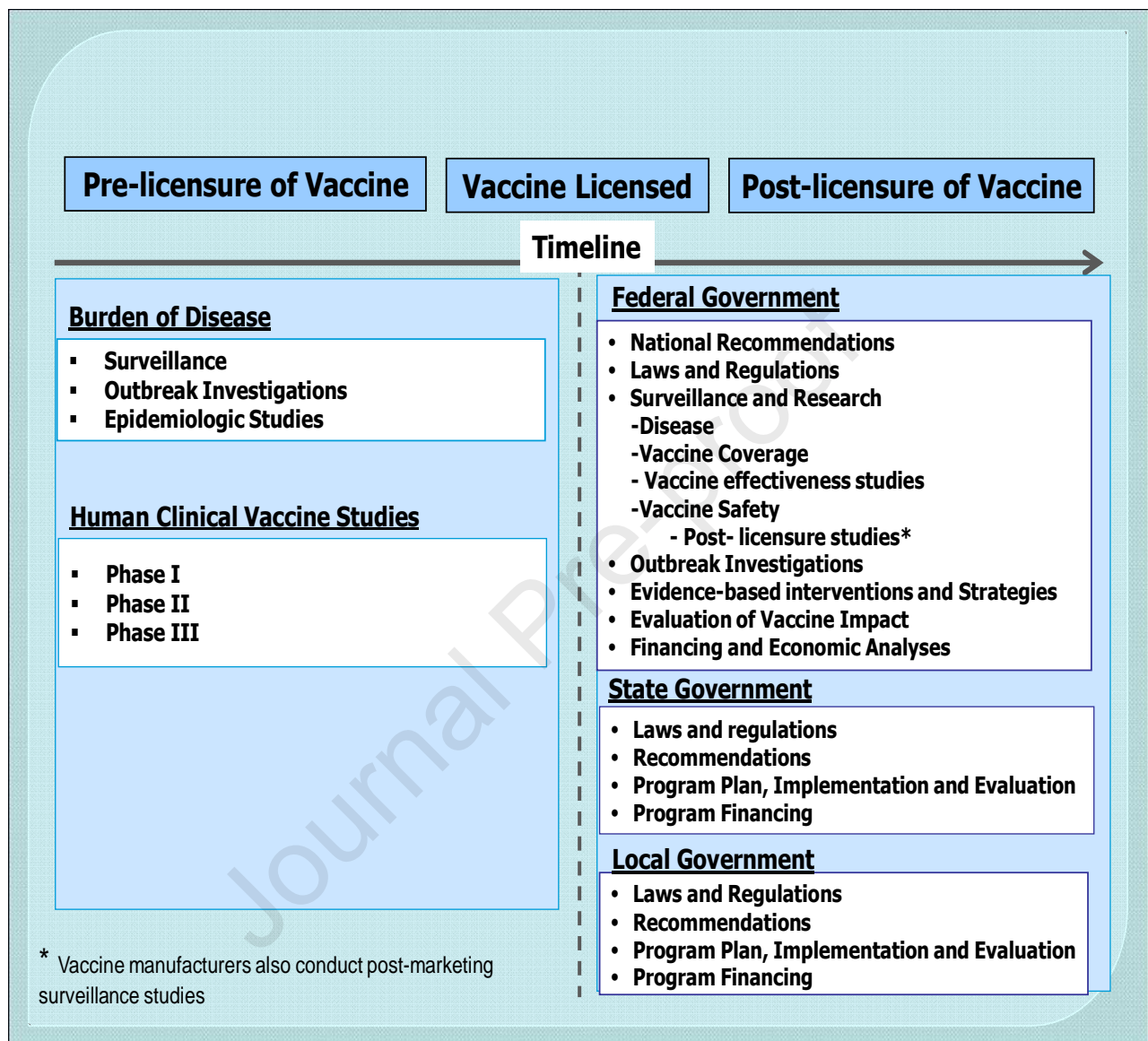
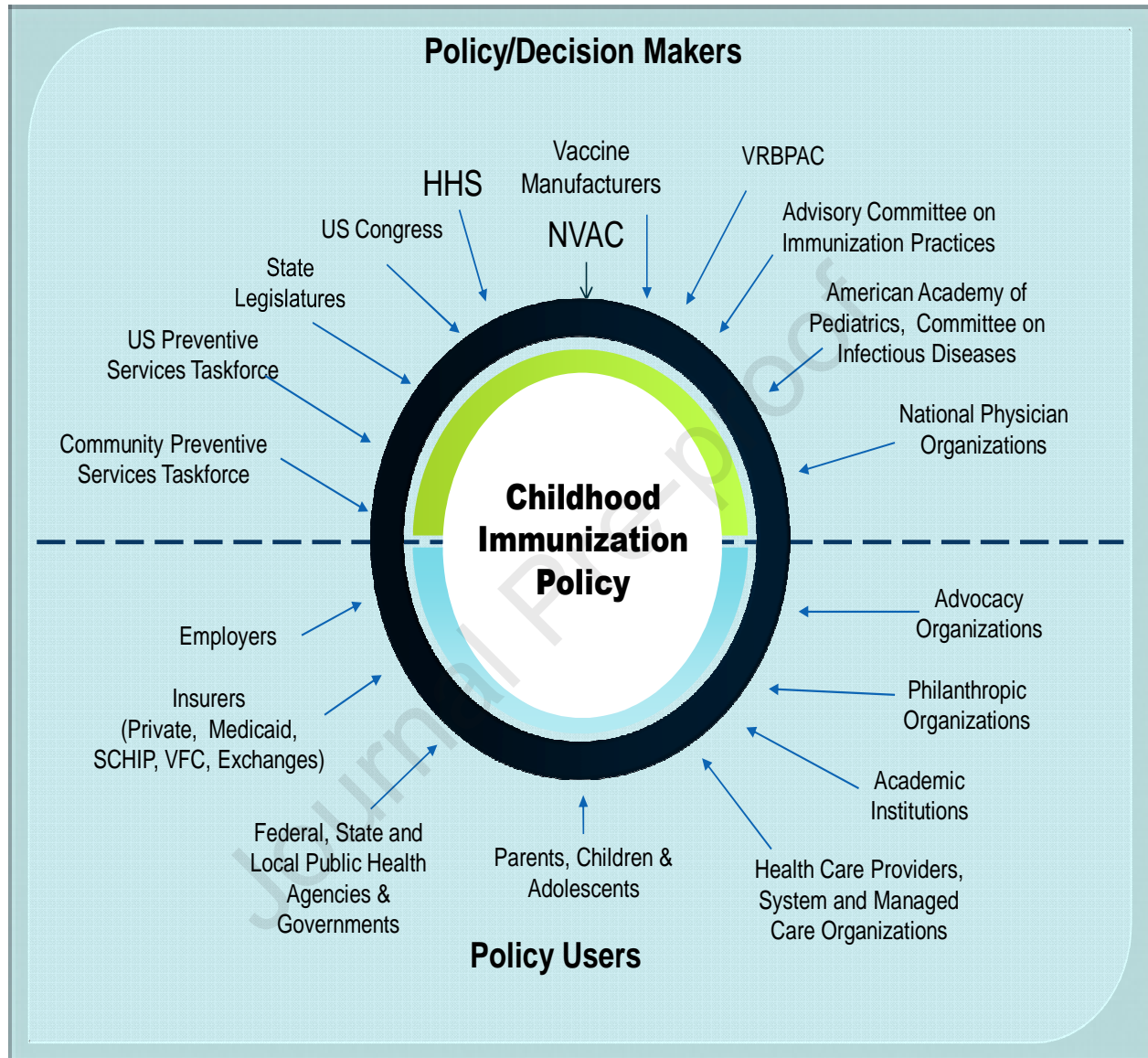
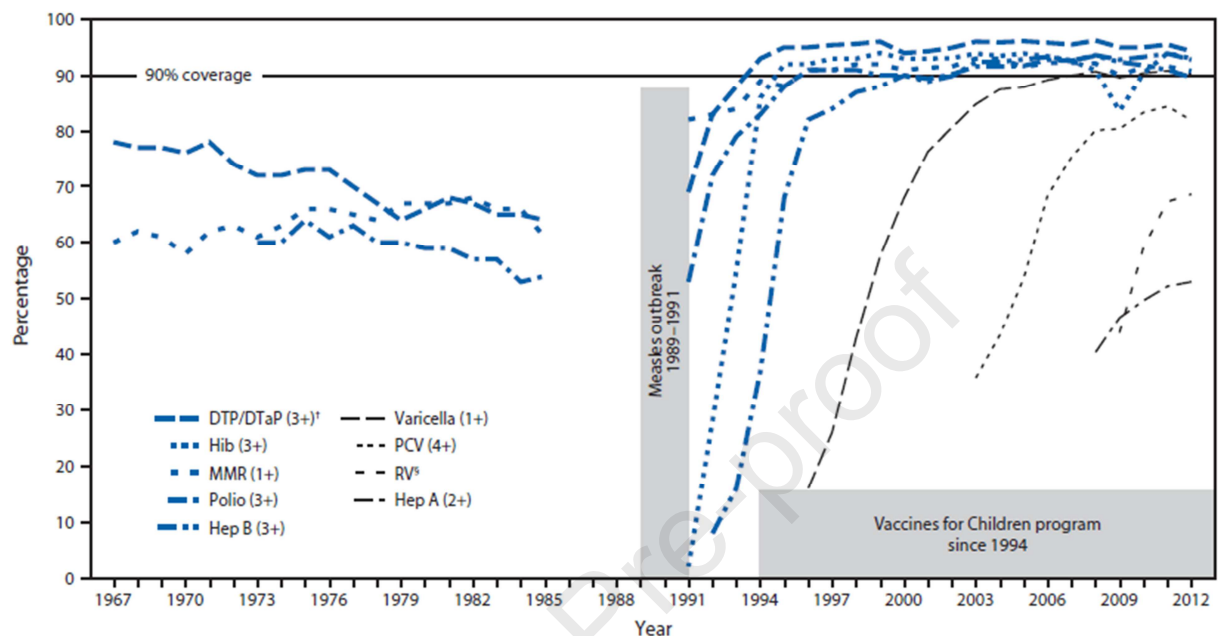


Figure 2. Key childhood immunization policymakers, practice decision makers and policy users



Abbreviations: HHS = Department of Health and Human Services, which includes the National Vaccine Program Office (NVPO), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), and National Institutes of Health (NIH); NVAC = National Vaccine Advisory Committee of the NVPO; VRBPAC = Vaccines and Related Biological Products Advisory Committee of the FDA; National Physician Organizations include those organizations other than the American Academy of Pediatrics (in figure) such as American Academy of Family Physicians (AAFP), American College of Obstetricians and Gynecologists (ACOG) and American College of Physicians (ACP); SCHIP = State Children's Health Insurance Program; and VFC = Vaccines for Children Program.

Figure 3. Vaccine coverage among preschool-aged children – United States, 1967-2012+



Abbreviations: DTP/DTPaP = diphtheria and tetanus toxoids and whole cell pertussis vaccine or diphtheria and tetanus toxoids and acellular pertussis vaccine; MMR = measles-mumps-rubella vaccine; Hib = *Haemophilus influenzae* type b vaccine; Hep B = hepatitis B vaccine; Varicella= varicella vaccine; PCV = pneumococcal conjugate vaccine; RV = rotavirus vaccine; Hep A = hepatitis A vaccine.

+ From the United States Immunization Survey (1967–1985), National Health Interview Survey (1991–1993), and National Immunization Survey (1994–2012), which is found in Whitney et al.⁶ Note: No data are available for 1986–1990. Children in the United States Immunization Survey and National Health Interview Survey were ages 24–35 months. Children in the National Immunization Survey were ages 19–35 months.

† Numbers in parentheses refer to the number of doses of that vaccine being reported in this figure.

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